General

Guideline Title

United Kingdom national guideline for gonorrhoea testing 2012.

Bibliographic Source(s)

Clinical Effectiveness Group. United Kingdom national guideline for gonorrhoea testing 2012. London (UK): British Association for Sexual Health and HIV (BASHH); 2012. 13 p. [51 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Ison C, Jungmann E, Bignell C. Gonorrhoea. In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 16-25.

Recommendations

Major Recommendations

Note from the British Association of Sexual Health and HIV (BASHH): This guideline complements the 2010 Health Protection Agency (HPA) document Guidance for gonorrhoea testing in England and Wales. This guideline should be read in conjunction with the BASHH United Kingdom (UK) national guideline for the management of gonorrhoea in adults 2010.

Definitions for the level of evidence (I-IV) and grade of recommendation (A-C) are provided at the end of the "Major Recommendations" field.

Major Changes in 2012 Guideline

Significant developments since the publication of the previous guideline in 2006 include:

1. Nucleic acid amplification tests (NAATs) are now used in many clinical services for detecting *Neisseria gonorrhoeae* and widespread clinical experience has been gained with these tests.
2. New NAATs with different nucleic acid targets and improved sensitivity and specificity have been developed and licensed; the Health protection Agency (HPA) has published guidance for gonorrhoea testing in England and Wales and the Health Protection Scotland (HPS) similar guidance in Scotland.
3. There have been clinical reports of treatment failures using many recommended treatments for gonorrhoea and increasing concern about reduced sensitivity of *N. gonorrhoeae* to third generation cephalosporins.

Major New Recommendations

1. NAATs are the test of choice for testing asymptomatic individuals for urethral or endocervical infection with *N. gonorrhoeae*.
2. NAATs are the test of choice for testing rectal and pharyngeal infection in men who have sex with men (MSM).
3. Positive NAATs from extragenital sites and low prevalence populations need confirmation by supplementary testing that uses a different nucleic acid target.
4. The re-introduction of test of cure is recommended as part of the routine follow-up of patients treated for gonorrhoea.
5. Testing by culture remains essential where infection persists after treatment and treatment failure is suspected.

Recommended Tests

No test offers 100% sensitivity and specificity and the prevalence of gonorrhoea in many genitourinary and sexual health clinics is less than 1%. The prevalence may vary between subgroups of patients even within the same clinic. The testing methodology used should give a positive predictive value (PPV) exceeding 90%. Laboratories used for testing should be appropriately accredited by a nationally approved accreditation scheme, notably by Clinical Pathology Accreditation (UK) Ltd (CPA) or equivalent.

There are two principal ways to detect *N. gonorrhoeae* – by detection of amplified nucleic acid and by culture. *N. gonorrhoeae* can also be visualized by microscopy of Gram stained specimens from the ano-genital mucosae which can be used to facilitate rapid diagnosis in symptomatic patients.

Recommendations

- Nucleic acid amplification tests (NAATs) are the recommended tests for urine in men, non-invasively collected samples (e.g., vulvovaginal swab) and for identifying rectal and pharyngeal infection in men-who-have-sex-with-men (MSM) (IIa, B). For endocervical and urethral specimens, NAATs offer higher sensitivity and less demanding specimen handling than culture but deny the opportunity for antimicrobial sensitivity testing.
- Culture remains a sensitive test for clinician taken genital specimens and is essential for patients with persisting symptoms or signs after treatment to exclude antimicrobial resistance.
- Microscopy of Gram-stained endocervical and urethral smears has low (40-60%) sensitivity in screening asymptomatic patients and is not recommended for routine practice.
- A culture should be taken in all cases of gonorrhoea diagnosed by NAAT's prior to antibiotics being given, if possible, so that susceptibility testing can be performed and resistant strains identified.

Recommended Sites for Testing

Mucosal sites associated with symptoms (discharge and/or pain) or signs (discharge and/or inflammation) should be tested for *N. gonorrhoeae*.

Screening

Current clinical practice in the United Kingdom (UK) for screening asymptomatic heterosexual individuals for gonorrhoea utilizes a single test and the sensitivity and convenience of NAATs: a first pass urine is collected from men and a vulvovaginal swab (which may be self taken) from women. Urine can be used in women but is sub-optimal. There is no data to confirm the adequacy of this approach. Culture testing in women identified the urethra as the only site of infection in 6%. Sampling the endocervix and urethra continues to be recommended when testing women by culture. There is little recent data quantifying the additional contribution of routinely taking rectal and pharyngeal specimens when screening women, although sampling should be considered at these sites where there is a history of direct exposure. There are no data on the minimum incubation period necessary to exclude infection but it is pragmatic to align it with the recommendation for chlamydia: that a test should be done when the patient presents and if the exposure was within the last two weeks, repeated two weeks after exposure.

Endocervix

In women, the endocervix is the principal site sampled, either directly during speculum examination or indirectly by a vulvovaginal swab. Samples taken directly from the endocervix are suitable for culture, NAATs and microscopy. Water based gel lubricants that are sterile and do not contain bacteriostatic or bactericidal additives appear not to affect cultures or NAATs for *N. gonorrhoeae*.

Urethra

In men, the urethra is the principal site sampled, either directly from the urethral meatus or indirectly in a first pass urine sample. Samples directly taken from the urethra are suitable for microscopy, culture and NAATs. For sampling, a loop or cotton-tipped swab is introduced 1 to 2 cm into the urethral orifice. A higher sensitivity for microscopy is reported for urethral samples taken with a plastic loop compared to those taken with a cotton-tipped swab.

In women, sampling the urethra is only recommended to complement testing with endocervical culture and after hysterectomy.

Rectum

Rectal testing should be dictated by symptoms and history of direct sexual exposure. The rectum can be sampled by culture and NAATs. NAATs offer significantly enhanced sensitivity compared with culture in MSM and are the test of choice in this patient population. Confirmatory testing is recommended for positive results. The use of NAATs on rectal samples may require local validation to comply with CPA accreditation. Anorectal samples from patients without symptoms may be obtained by blindly passing a moist swab 2 to 4 cm into the anal canal, using lateral pressure to try and avoid any faecal mass (IIIB). Swabs with heavy faecal contamination should be discarded. In symptomatic patients, proctoscopy may aid diagnosis and allow specimens to be obtained under direct vision. Obtaining smears under direct vision improves the low sensitivity of microscopy (IIIC) to aid immediate diagnosis.

Oropharynx

Oropharyngeal testing should be dictated by symptoms and history of direct sexual exposure. For men, the pharynx should be sampled if the man has been the active provider of fellatio, but not if he is only the active provider of cunnilingus. Specimens are obtained by wiping a swab over the posterior pharynx, tonsils, and tonsillar crypts. Samples can be tested by culture (although sensitivity is low) and NAATs. NAATs are not approved for testing for *N. gonorrhoeae* in the pharynx but offer significantly enhanced sensitivity compared with culture in MSM and other high risk individuals. They are the test of choice in these patient populations and confirmatory testing is recommended for positive results. The use of NAATs on pharyngeal samples may require local validation to comply with CPA accreditation.

Urine

Urine is an easily obtained non-invasive sample and is the sample of choice when testing asymptomatic men using a NAAT. The first 15 to 30 mls of urine is collected after urine has been held for at least an hour. Urine is not suitable for culture. In women, the sensitivity of urine testing by NAATs is lower than vulvovaginal or endocervical swabs and urine is not a specimen of choice in women (IIB).

Vagina

Patient-taken vulvovaginal swabs and clinician-taken endocervical swabs are equally suitable for detecting *N. gonorrhoeae* when tested by NAATs. Vulvovaginal swabs are the sample of choice for screening asymptomatic women for gonorrhoea.

Neisseria gonorrhoeae may infect the vaginal mucosa of prepubertal girls because the vagina is lined with columnar epithelium in pre-pubertal girls. Vaginal samples should be cultured in these circumstances in view of the implications of the diagnosis and to provide diagnostic certainty.

Bartholin's Duct

When a Bartholin's abscess is present, purulent material expressed from the duct may be cultured and stained for microscopy.

Ophthalmic and Systemic Sites

Ophthalmic samples are suitable for culture. Specimens are obtained after cleaning excess exudates by wiping a swab over the lower eye lid. NAATs are not licensed for this site and there is no data to validate their use on the conjunctiva.

Proving infection in patients with suspected disseminated gonococcal infection (DGI) can be difficult. The diagnosis of DGI is made on the basis of positive blood or synovial culture or, in a patient with the typical clinical syndrome and negative blood or synovial culture results, on the basis of gonococci isolated from another site. Genital and pharyngeal samples should be taken and have a higher yield in identifying the presence of *N. gonorrhoeae* than blood cultures (IIIC).

Factors Which Alter Tests Recommended or Sites Tested

Sexual History

Testing in heterosexual men and women focuses on the genital tract. Infection may be asymptomatic and all sexually active heterosexuals requesting

screening for sexually transmitted infection at a genitourinary medicine clinic should receive a genital tract test for gonorrhoea. The prevalence of pharyngeal infection in patients attending genitourinary clinics in the UK is believed to be low and there is no evidence to support routine pharyngeal testing of heterosexuals who disclose oro-genital sexual activity. Data from a high-risk female population in the Netherlands show a prevalence of isolated pharyngeal infection of <0.3%. Rectal testing in women practicing anal sex is indicated in the presence of symptoms consistent with rectal infection and after sexual assault with anal penetration. The additional contribution of a rectal test to a vulvovaginal or endocervical NAAT to determine the infection status of asymptomatic women is small even in a high-risk population. A history of condom use for intercourse is not an indication to omit testing for gonorrhoea.

Risk Groups

- Men who have sex with men
  Tests should be taken from all sites (urethra, rectum, and oropharynx) potentially exposed to infection as directed by the sexual history (recommendation C). Rectal infection may be acquired by transmission from the oropharynx in the absence of penetrative anal intercourse.

- Sex workers
  Test all sites potentially exposed to infection as indicated by sexual history. A history of condom use should not deter testing at exposed sites.

- 'Young' patients
  Testing in post-pubertal young men and women follows that in adults. Young people may be intimidated by the prospect of invasive tests and may prefer non-invasive options when available, notably urine testing. Cultures and implementation of chain of evidence should be considered if there is prospect of legal proceedings for sexual abuse.

Other Groups

- Pregnant women
  Screening tests as for heterosexual women.

- Women with history of hysterectomy
  A urethral swab for culture offers a better yield than high vaginal culture. No comparative data was found on testing urine, urethral swab, and vaginal swabs by NAATs.

- Patients who are known contacts of gonorrhoea
  Test all sites potentially exposed to infection as indicated by the sexual history. Microscopy may be worthwhile even if the patient is asymptomatic.

Recommendation for Frequency of Repeat Testing in an Asymptomatic Patient

The minimum time interval between exposure and when to test for gonorrhoea has not been determined (see above). Symptoms may develop within a few days and the incubation period for detection by culture is said to be 2 to 7 days.

Repeat testing should relate to risk rather than to a prescribed frequency. The prevalence of gonorrhoea in the general population is low but there are linked population subgroups at higher risk of infection and re-infection. The chance of contracting gonorrhoea depends largely on membership or contact with these subpopulations. A past history of gonorrhoea is a strong risk factor for re-infection. Re-infection rates of 0 to 30.8% have been reported in follow-up studies and about a third of patients with gonorrhoea in England and Wales have a history of previous infection. There is no compelling evidence to support frequent checks in sex workers, who have almost universal condom use at work. No general recommendation on the frequency of repeat testing in asymptomatic patients is suggested. Sexual health checks in relation to new risk exposures are self-evident and commended.

Recommendation for Test of Cure

Progressive creep in minimal inhibitory concentration (MIC) to cephalosporins and reported treatment failures with ceftriaxone and cefixime indicate that microbiological cure can no longer be presumed with currently recommended treatments. Test of cure is recommended following treatment for all gonococcal infections (IVC). This is to identify treatment failure, emerging resistance which is predicted to occur on the basis of the past capability/history of *N. gonorrhoeae* and because susceptibility results that indicate potential failure to ceftriaxone and cefixime are not yet defined.

Where resource or practical considerations require test of cure to be selective rather than universal, then the following patients should be prioritized –

- Persisting symptoms or signs
- Pharyngeal infection (all treatments are less effective at eradicating pharyngeal infection)
- Treatment with anything other than the first-line recommendations
- Pregnant women

Method and Timing of Test of Cure

There is a lack of evidence on optimal timing for test of cure and method of testing. Current opinion and pragmatic considerations suggest that where there are persisting symptoms or signs, testing with culture should be performed at least 72 hours after completion of therapy.

If asymptomatic, test with NAAT's where available followed by culture if positive. Test two weeks after completion of antibiotic therapy.

Definitions:

Level of Evidence

Ia Meta-analysis of randomised controlled trials

Ib At least one randomised controlled trial

IIa At least one well designed controlled study without randomisation

IIb At least one other type of well-designed quasi-experimental study

III Well designed non-experimental descriptive studies

IV Expert committee reports or opinions of respected authorities

Grading of Recommendation

A. Evidence at level Ia or Ib
B. Evidence at level IIa, IIb, III
C. Evidence at level IV

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Gonorrhoea

Guideline Category

Diagnosis

Evaluation

Risk Assessment

Screening

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

Pathology

Urology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Clinical Laboratory Personnel

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To offer recommendations on gonorrhoea testing for use in specialist sexual health clinics in the United Kingdom (UK)
- To provide principles applicable to other healthcare settings where screening or testing for *Neisseria gonorrhoeae* is undertaken

Target Population

Individuals in the United Kingdom with or at risk for gonorrhoea

Interventions and Practices Considered

1. Nucleic acid amplification tests (NAATs)
2. Culture for *Neisseria gonorrhoeae*
3. Microscopy for intracellular Gram-negative diplococci
4. Confirmatory testing of positive NAATs from extragenital sites and low prevalence populations
5. Sampling by loop or cotton-tipped swab culture of mucosal sites, as appropriate, including endocervix, urethra, rectum, oropharynx, urine, vagina, Bartholin's duct, and ophthalmic and systemic sites
6. Special considerations for testing of heterosexual women, heterosexual men, men who have sex with men, women who have had a hysterectomy, 'young' men and women, pregnancy, sex workers, victims of sexual assault, and sexual contacts of individuals with gonococcal infection
7. Frequency of repeat testing in asymptomatic patients
8. Patient assessment after treatment, including test of cure

Major Outcomes Considered

- Test sensitivity and specificity
- Test positive predictive value (PPV)
- Prevalence of gonorrhoea

- Re-infection rate

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

To update this guideline, a Medline search was conducted using the terms "gonorrhoea AND testing", "gonorrhoea AND diagnosis", and "gonorrhoea AND screening" covering the period January 2006 to December 2010. Duplicates were removed and titles and abstracts in the English language were screened (663). Full articles testing for gonorrhoea in-vitro and in clinical trials were obtained and reviewed. The Cochrane collaboration databases (www.cochrane.org) and the Centers for Disease Control and Prevention (CDC) Sexually Transmitted Disease (STD) treatment guidelines 2010 (www.cdc.gov/std) were reviewed.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Level of Evidence

Ia Meta-analysis of randomised controlled trials

Ib At least one randomised controlled trial

IIa At least one well designed controlled study without randomisation

IIb At least one other type of well-designed quasi-experimental study

III Well designed non-experimental descriptive studies

IV Expert committee reports or opinions of respected authorities

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Guideline development is undertaken by a multi-disciplinary writing committee with membership determined in a transparent manner. The chair is chosen by the Clinical Effectiveness Group (CEG). The CEG lead then discusses with the chair what suggestions they might have for members from other disciplines. The additional members of the group are then invited by the CEG. Writing committee membership includes relevant professional groups (for example, genitourinary medicine physicians, nurses, health advisors, pharmacists, microbiologists, and other professionals from allied specialties as appropriate) and when relevant this will involve working with the appropriate British Association for Sexual Health and HIV (BASHH) Special Interest Group (SIG) and the BASHH audit group.

This guideline was developed with involvement of the Bacterial Special Interest Group of BASHH, a group of clinicians and microbiologists with an interest in sexually-transmitted infections (STIs). There was no patient or public involvement.

Recommendations are formulated with consideration of their health benefits, side effects and risks, with evidence presented in the guideline that these issues have been addressed. Each recommendation is linked to the supporting evidence with a list of relevant references in the original guideline document.

Consideration is given to pragmatic and organisational issues relevant to the guideline. This is sought during and may emerge from the piloting of the guideline.

The authors consider the financial cost implications of recommendations made. Where disagreement arises within the writing committee with regard to recommendations the chair attempts to resolve these (for example by a voting system or formal consensus method). The process is documented and reported to the CEG editor. When this is not possible the CEG will review the evidence.

Rating Scheme for the Strength of the Recommendations

Grading of Recommendation

A. Evidence at level Ia or Ib
B. Evidence at level IIa, IIb, III
C. Evidence at level IV

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was posted on the British Association of Sexual Health and HIV (BASHH) website for 3 months for consultation and comments taken into account by the authors and the Clinical Effectiveness Group (CEG) in preparing the final version.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Accurate diagnosis of gonorrhea

Potential Harms

Not stated

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Clinical Effectiveness Group. United Kingdom national guideline for gonorrhoea testing 2012. London (UK): British Association for Sexual Health and HIV (BASHH); 2012. 13 p. [51 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Aug (revised 2012)

Guideline Developer(s)

British Association for Sexual Health and HIV - Medical Specialty Society

Source(s) of Funding

No specific or external funding was sought or provided in the development of this guideline.

Guideline Committee

Clinical Effectiveness Group (CEG)

Composition of Group That Authored the Guideline

Principal Authors: Chris Bignell, Consultant Physician in Genitourinary Medicine, Nottingham University Hospitals NHS Trust; Catherine Ison, Professor of Microbiology, STBRL, Health Protection Agency, UK; Mark FitzGerald, Lead Editor, Consultant Physician in Genitourinary Medicine, Musgrove Park Hospital, Taunton

Clinical Effectiveness Group (CEG) Members: Dr Keith Radcliffe (*Chair*), Consultant Physician in Genitourinary Medicine Whittall Street Clinic; Dr David Daniels, West Middlesex University Hospitals NHS Trust, Sexual Health Clinic West Middlesex Hospital, Isleworth; Dr Mark FitzGerald, Consultant Physician in Genitourinary Medicine, Musgrove Park Hospital, Taunton; Dr Margaret Kingston, Consultant Physician in GU Medicine, Manchester Centre for Sexual Health, The Hathersage Centre, Manchester; Dr Neil Lazaro, Associate Specialist in GU Medicine, Royal Preston Hospital, Preston; Dr Gill McCarthy, Consultant Physician in GU Medicine, Kingston Hospital NHS Trust, Wolverton Centre for Sexual Health, Kingston Upon Thames; Dr Ann Sullivan, Consultant Physician in Genitourinary Medicine, Chelsea & Westminster Healthcare NHS Trust, John Hunter Clinic

Financial Disclosures/Conflicts of Interest

Each of the authors has declared they have no conflict of interest.

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Guideline Availability

Electronic copies: Available from the British Association for Sexual Health and HIV Web Site .

Availability of Companion Documents

The following is available:

- British Association for Sexual Health and HIV: framework for guideline development and assessment. London (UK): British Association for Sexual Health and HIV; 2010. 18 p. Electronic copies: Available in Portable Document Format (PDF) from the BASHH Web site .

Additionally, auditable outcome measures can be found in the original guideline document .

Patient Resources

The following is available:

- A guide to gonorrhoea. Patient information leaflet. London (UK): British Association for Sexual Health and HIV; 2012 Jan. 2 p. Electronic copies: Available in Portable Document Format (PDF) from the British Association for Sexual Health and HIV (BASHH) Web site .
- A BASHH guide to gonorrhoea. Gonorrhoea - the basics. Electronic copies: Available from the BASHH Web site .

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NGC Status

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